Transurethral Balloon Laser Enhanced Thermotherapy in the Canine Prostate

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Background and Objective: **Hyperthermia is performed for prostate cancer. We examined the selective induction of coagulonecrotic changes in the objective area of the canine prostate in enhancing the effect of hyperthermia and treating the target area with transurethral balloon laser enhanced thermotherapy (TUBAL-ET) using a light absorbent material.**
Study Design/Materials and Methods: **The heat exchange of ultrafine carbon particles after laser irradiation was observed in a phantom study using thermography. The carbon solution was injected at the right prostatic lobe in dogs and TUBAL-ET was performed.**
Results: **The charcoal absorbed the Nd:YAG laser energy and apparently converted it into thermal energy in the phantom study by thermographic observation. TUBAL-ET induced coagulonecrotic changes only at the area at which carbon had been injected in the prostate gland. The necrotic tissue was almost absorbed at four weeks after treatment.**
Conclusions: **TUBAL-ET induces tissue damage at the target area in the prostate gland. Lasers Surg. Med. 21:321–328, 1997.**

Key words: thermotherapy; prostate; canine; TUBAL-ET

INTRODUCTION

Transurethral balloon laser hyperthermia (TUBAL-H) has been performed for the treatment of patients with chronic prostatitis [1]. TUBAL-H was performed using PROSTALASE™ system (SLT-Japan, Co., Ltd., Hachioji, Japan) which transurethrally generates an Nd:YAG laser beam directed at the prostatic tissue in a spindle pattern via an internal laser probe. This system is designed for hyperthermia and thermotherapy preserving the urethral tissue which is cooled to below 38°C under urethral cooling with the intraballoon circulation of cooled water [1–3].

Prostate cancer is a common disease in elderly men, and in more than 50% of the patients it is first diagnosed at the locally advanced stage or when metastatic lesions are already present. Hormonal or radiation therapy is effective for the localized tumor, but the recurrent or advanced cancer is often unresponsive to conventional therapy [4]. Transurethral balloon laser thermotherapy has been performed for the patients with benign prostatic hyperplasia, coagulative necrosis was induced in the prostate gland, and severe adverse effects were not observed [2,3]. The present basic study in dogs demonstrated that, as a means of enhancing the effect of thermotherapy and of treating the target area, transurethral balloon laser enhanced thermotherapy (TUBAL-ET) using a light absorbent material selectively induces coagulonecrotic changes in the objective area of the prostate.

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MATERIALS AND METHODS

Agent

Ultrafine particles of carbon (Carbon Black), used as a light absorbent material, and polyvinylpyrrolidone K30 (PVP K30), used to stabilize the dispersion of carbon, were purchased from Katayama Chemical Industries Co., Ltd. (Osaka, Japan). The solution of carbon contained 10 mg of charcoal and 4 mg of PVP K30 per ml of saline.

Observation of Exchange to Heat of Carbon by Thermography

The temperature distribution was measured using a phantom composed of fish cake (kamaboko) made in Japan; because of its protein content, fish cake absorbs an Nd:YAG laser beam in a manner similar to the prostatic tissue. The measurement of the temperature in a phantom using thermography (Conpact Thermo TVS-2000ST, Nippon Avionics Co., Ltd., Tokyo, Japan) was already reported [6]. The balloon laser probe was placed in the fish cakes and 0.3 ml of carbon solution was injected into the phantom at 5 mm from the balloon surface. The phantom was irradiated using the balloon laser probe. As a control, PVP K30 solution (0.3 ml) was placed in the phantom and irradiated. The balloon probe was 3 cm long, the laser power was 40 watts, the pressure of the intra-balloon cavity was maintained at 0.7 kg/cm^2, the temperature of the circulating water was 10°C, and the circulation rate was 180 ml/min. Changes of the temperature were observed using thermography in the longitudinal and transverse planes, and the temperature was measured at 3 minutes after laser radiation [5].

Transurethral Balloon Laser Enhanced Thermotherapy

Sixteen male mongrel dogs, weighing 9–15 kg (average weight, 12.5 kg), were used for TUBAL-ET. A perineal urethrostomy was performed before treatment. The non-shielded balloon with a laser probe was placed into the prostatic urethra via the perineal urethrostomy. An 18 gauge needle was inserted via a perineal route into the prostatic tissue, to the right of the urethra, and placed at 5 mm depth from the urethral surface in the mid-portion of the prostate using rectal ultrasound guidance (SAL-77B, Toshiba, Tokyo, Japan). Carbon solution (0.3 ml) was injected into the prostatic tissue via the needle. For measurement the temperature of the prostatic tissue at the injected area during treatment, a thermocouple was inserted into the same position through the interior cavity of the needle. An other thermocouple was perineally inserted at 5 mm depth from the urethra to its left. The temperature of the urethral surface was measured by a thermocouple at the balloon surface, and that of the rectum was measured by a thermocouple at the anterior wall of the rectum [5]. The thermocouple (SS30–200 type K, Anritsu Meter Co., Ltd., Tokyo, Japan) was coated by gold not to absorb the laser light [6]. The temperature of the urethra was maintained at between 36–38°C during treatment by a computer feedback system of this device, and that of the rectum was maintained at 40–42°C.

TUBAL-ET was performed for ten minutes after the rectal temperature had reached 40°C. The balloon probe was 2 cm long, the laser power used was 40 watts, the pressure of the intra-balloon cavity was kept at 0.5 kg/cm^2, the temperature of the circulating water was 10°C, and the circulation rate was 150 ml/min. These conditions formed the temperature distribution in dog's prostate almost similar to those in the phantom which was irradiated as described above [6]. After treatment, the dogs urinated spontaneously. A single 0.1 ml/kg bolus of benzylpenicillin (Duoppen, Pitman-Moore Ireland, Bray, Ireland) was administered intramuscularly. Histological examination was performed at one day (three dogs), one week (three dogs), and four weeks (seven dogs) after treatment. Saline (0.3 ml) in one dog or PVP K30 solution (0.3 ml) in two dogs was injected into the prostatic tissue, TUBAL-ET was performed as a control, and the prostate was examined after one week. The prostate was removed, and fixed in 20% buffered formalin. Serial sections were cut perpendicular to the urethra and stained with hematoxylin and eosin for examination.

RESULTS

Observation of the Temperature Distribution in a Phantom by Thermography

The temperature distribution in the phantom is shown in Figure 1. Examination of the phantom in the longitudinal plane disclosed that the distribution profile was elliptical and that the region of greatest tissue temperature elevation was distributed bilaterally at a depth of about 5

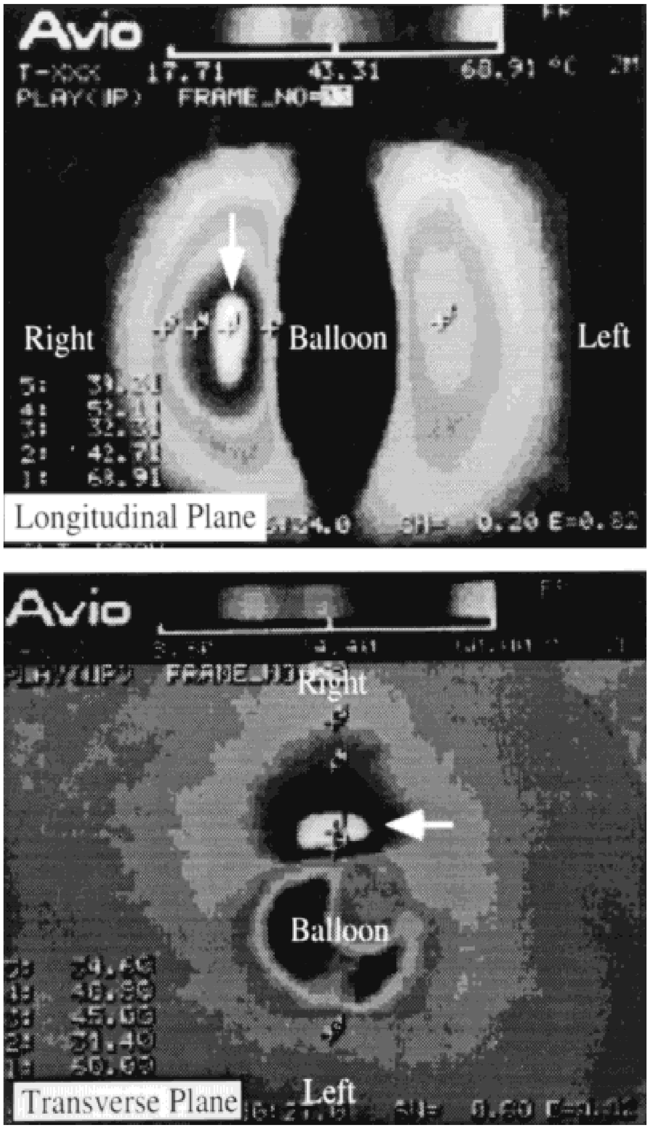

Fig. 1. Observation of the temperature distribution in the phantom using thermography. The temperature was highest at the area (arrow) injected with the carbon solution.

mm from the balloon surface. The temperature elevation was highest at the area injected with carbon. The temperature difference between the injected and non-injected areas was average 26.2°C. In the transverse plane, the temperature distribution demonstrated a cylindrical pattern. The temperature elevation was highest at the area injected with carbon. The temperature difference between the injected and non-injected areas was average 28.6°C. The temperature difference was not observed at between PVP K30 injected and non-injected areas. The carbon absorbed the Nd:YAG laser energy, and the temperature was selectively elevated at the injection area of the phantom.

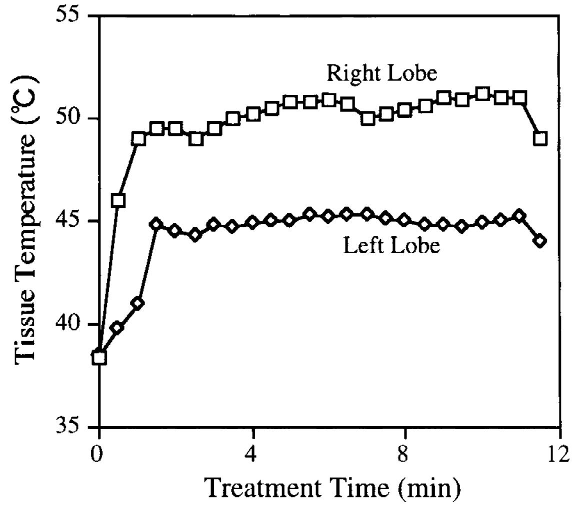

Fig. 2. An example of changes of tissue temperature in the canine prostate during TUBAL-ET. The temperature at the area injected with the carbon solution (right lobe) was higher than that at the non-injected area (left lobe). The average difference was 7.6°C during treatment.

Changes of the Tissue Temperature in the Prostate During TUBAL-ET

The change during treatment in the tissue temperature at the right and left sides of the prostate is shown in Figure 2. The rectal temperature reached 40°C within one minute thirty seconds (average time, one minute) after the start of treatment. The temperature at the right side, into which the carbon solution had been injected, showed more rapid elevation compared with that at the left side, reached about 50°C, and remained constant at about 51°C during treatment. The temperature at the left side elevated more slowly and remained constant at 44.5°C. The tissue temperature at the right and left side ranged from 46–70°C (average temperature, 49.9°C) and from 40.5–44.5°C (average temperature, 42.3°C), respectively and the difference between the averages in thirteen dogs was 7.6°C.

Histological Changes after TUBAL-ET

The total joules (J) during treatment ranged from 10,052J–17,472J (average, 12,573J). The weight of the prostate gland ranged from 7.5g–27g (average weight, 12.1g). At one day after treatment, coagulonecrosis was observed in the prostatic epithelia and stroma at the right (car-

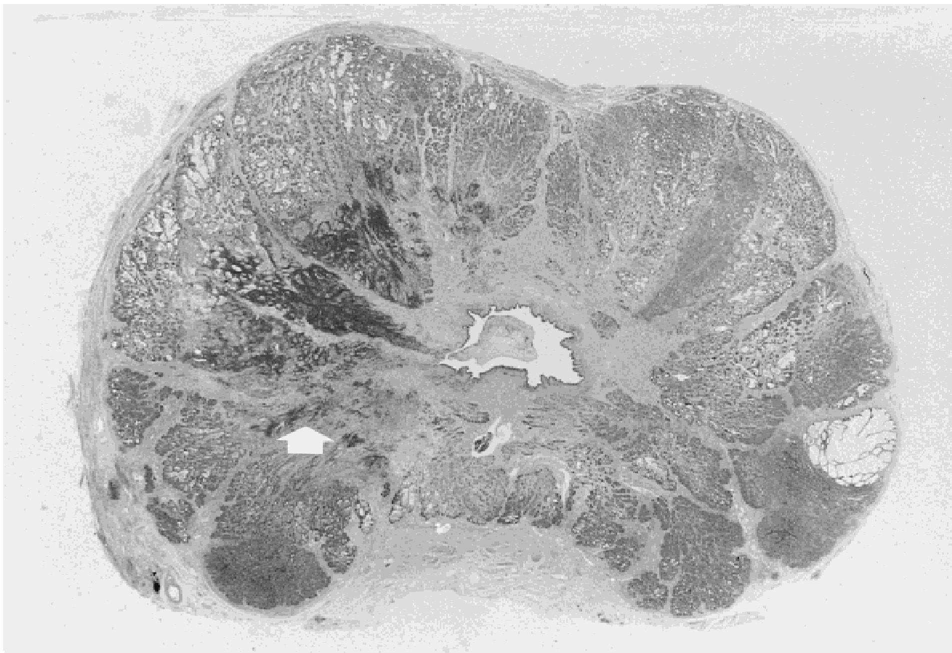

Fig. 3. Dissecting macroscopic view of transversely sectioned prostate at one day after TUBAL-ET. Coagulonecrotic changes were observed only at the right lobe (arrow), which had been injected with the carbon solution. Hematoxylin and eosin staining.

bon-injected) side. Hemorrhage in the stroma was also observed around the necrotic area (Figs. 3 and 4). At the left side, no coagulonecrotic change other than edematous change in the stroma was observed. At one week after treatment, a cavity containing necrotic tissue had formed at the right lobe in all dogs (Figs. 5 and 6), but there was no tissue damage at the left lobe. Many histiocytes phagocytizing carbon particles and inflammatory cells were observed to have infiltrated into the stroma. There was no coagulative necrosis and cavity formation in the prostate gland in saline and PVP K30 injected groups. At four weeks after treatment, the coagulonecrotic tissue in the right lobe was absorbed and the cavity had markedly shrunk (Figs. 7 and 8). Slight coagulonecrosis was remained in three of seven dogs, and inflammatory cells had invaded the stroma (Fig. 9). There was no tissue damage in the left lobe in any dog.

DISCUSSION

The carbon particles used in the present study, measuring 21 mμ in diameter, have the property of adsorbing to various agents such as mitomycin C. Carbon particles adsorbed to mitomycin C have been injected into the lymph nodes in patients with D1 or D2 gastric cancer during gastrectomy, and the survival of these patients was significantly improved compared with that in the control group [7]. From their study, there was no adverse effect of carbon solution, and it was thought that carbon solution might be usable in its clinical application. The present study demonstrated that the charcoal absorbs Nd:YAG laser energy and converts it to thermal energy when it is irradiated by the laser beam. The thermographic observation in the phantom revealed that the temperature at the area injected with carbon was selectively elevated compared to that at the non-injected area. Charcoal thus absorbs Nd:YAG laser energy and converts it to thermal energy.

The tissue temperature in the canine prostate showed more rapid elevation at the right, carbon-injected, lobe than at the left lobe, and the average difference was 7.6°C during treatment. The difference of temperature in the phantom was about 27.4°C. The difference in vivo was small, and the reason is thought to be the cooling effect of the blood circulation. The tissue temperature in the prostate during TUBAL-H was elevated to 43°C in patients with prostatitis [1]. We estimated that, had the charcoal been used during TUBAL-H, the temperature at the injected area would have been elevated to more than 50°C. Coagulonecrosis was induced in adenoma of the human prostate during treatment elevating the temperature of the adenoma to about 50°C for 40 min-

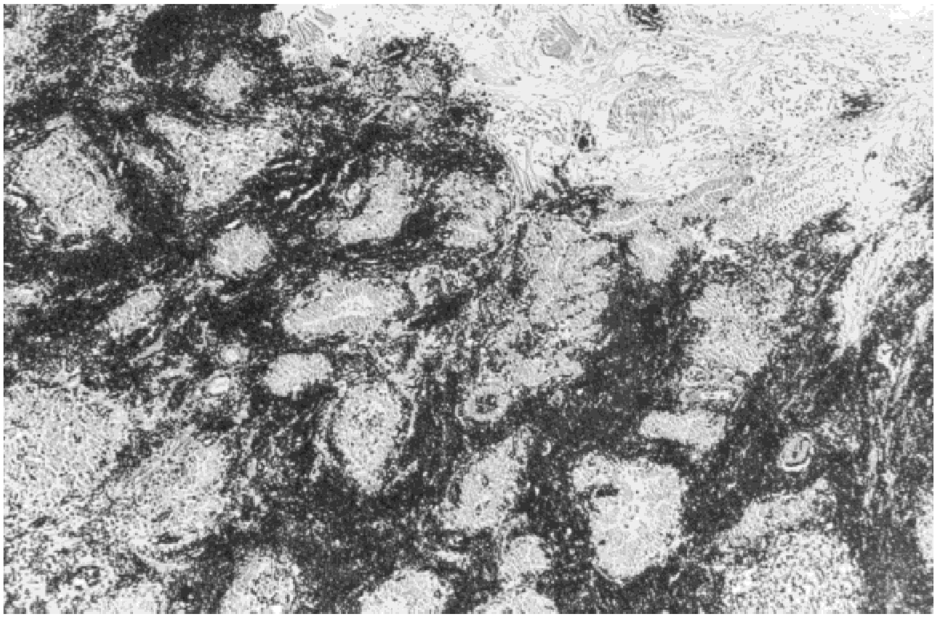

Fig. 4. Photomicrograph of the right prostatic lobe at one day after TUBAL-ET. Coagulonecrosis of the prostatic epithelia and the stroma and the hemorrhage in the stroma were observed. Carbon particles dispersed in the stroma were not detected under a light microscope. Hematoxylin and eosin staining, ×88.

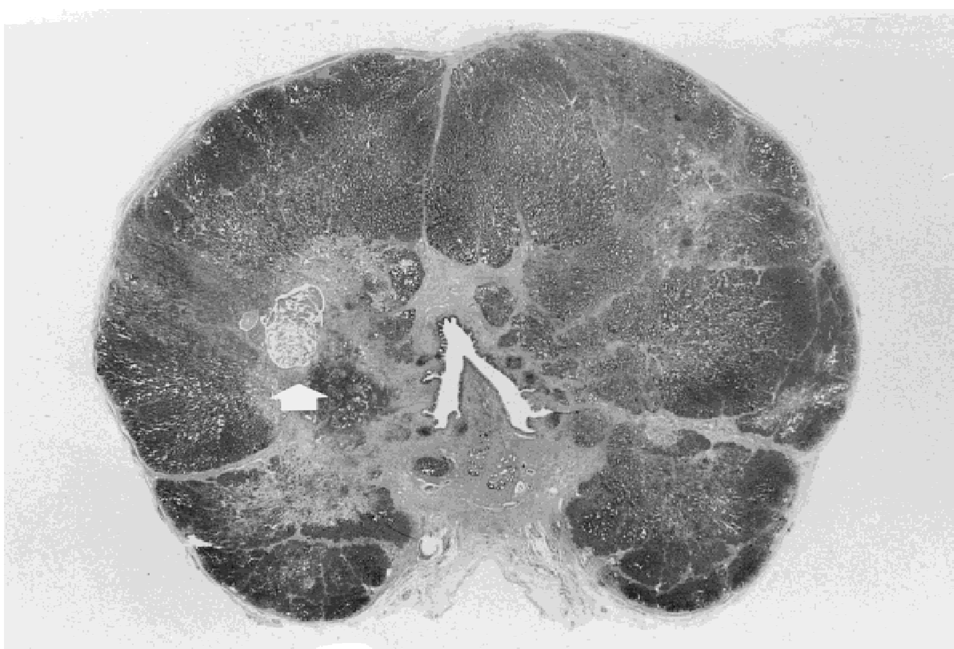

Fig. 5. Dissecting macroscopic view of transversely sectioned prostate at one week after TUBAL-ET. A cavity containing necrotic tissue was formed at the right lobe (arrow). Hematoxylin and eosin staining.

utes [2]. Cancer cells are known to be much more sensitive to hyperthermia than normal cells [8]. Given these data, we speculated that TUBAL-ET using a light absorbent material such as carbon would more satisfactorily destroy cancer cells.

The present study demonstrated that TUBAL-ET induced coagulonecrotic changes in the area injected with carbon, which was administered at the target lesion under transrectal ultrasound guidance. The necrotic tissue in the canine prostate was almost absorbed at four weeks after treatment. TUBAL-H is a safe method and

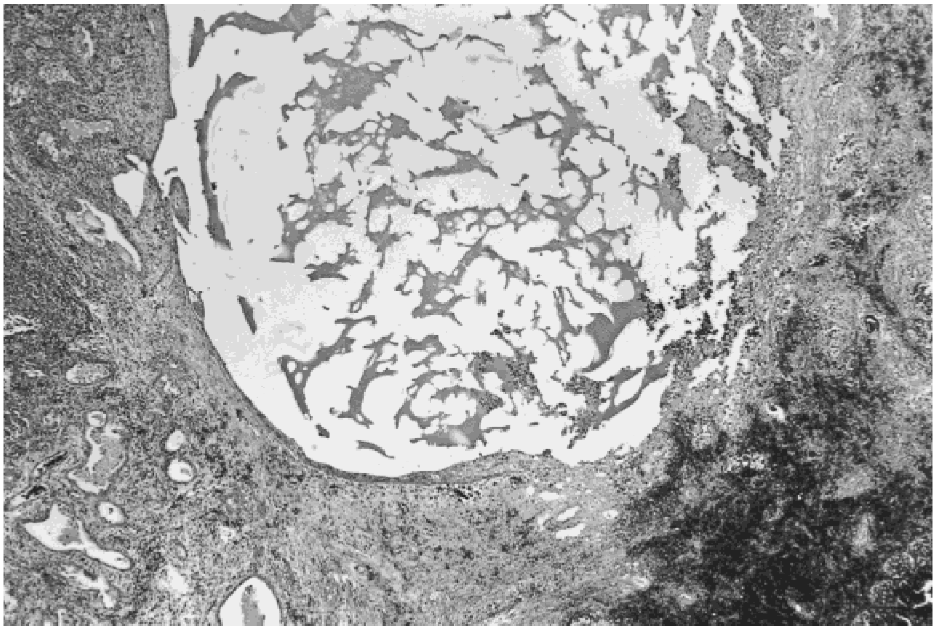

Fig. 6. Photomicrograph of the right prostatic lobe at one week after TUBAL-ET. A cavity containing necrotic tissue has formed, and part of it has become re-epithelialized. Necrosis of the stroma is observed around the cavity. Hematoxylin and eosin staining, ×35.

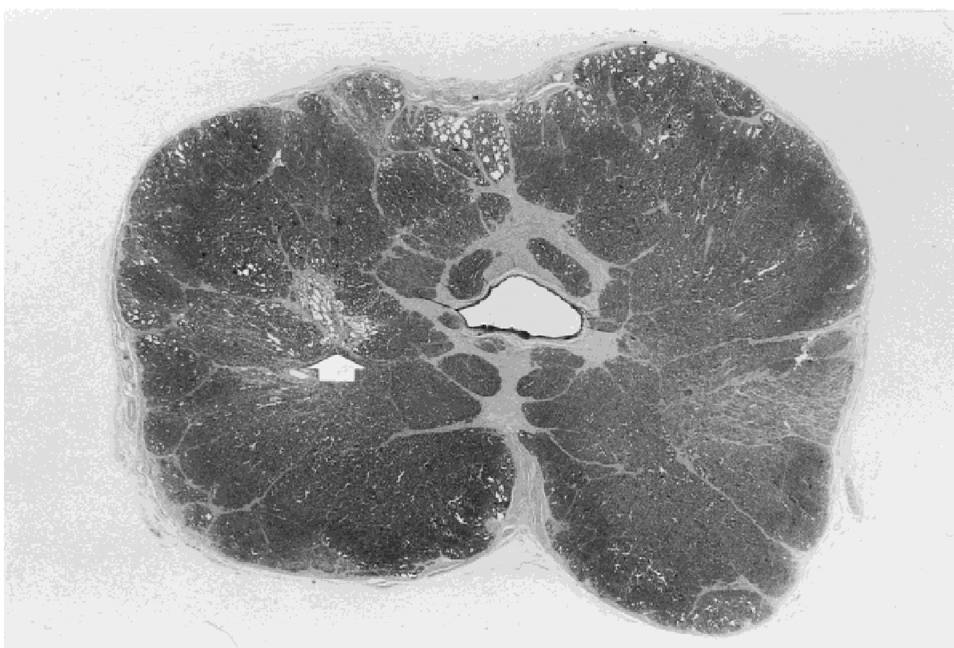

Fig. 7. Dissecting macroscopic view of transversely sectioned prostate at four weeks after TUBAL-ET. The necrotic tissue in the right lobe was absorbed and the size of right lobe was slightly smaller than that of the left lobe. Hematoxylin and eosin staining.

has low complication rates, because the urethral mucosa is preserved by urethral cooling [1–3]. As patients with prostate cancer are frequently elderly men, having other disorders, and in view of the foregoing, we believe that TUBAL-ET, when it can be applied, may be a useful treatment method for prostate cancer, especially for recurrent cancer.

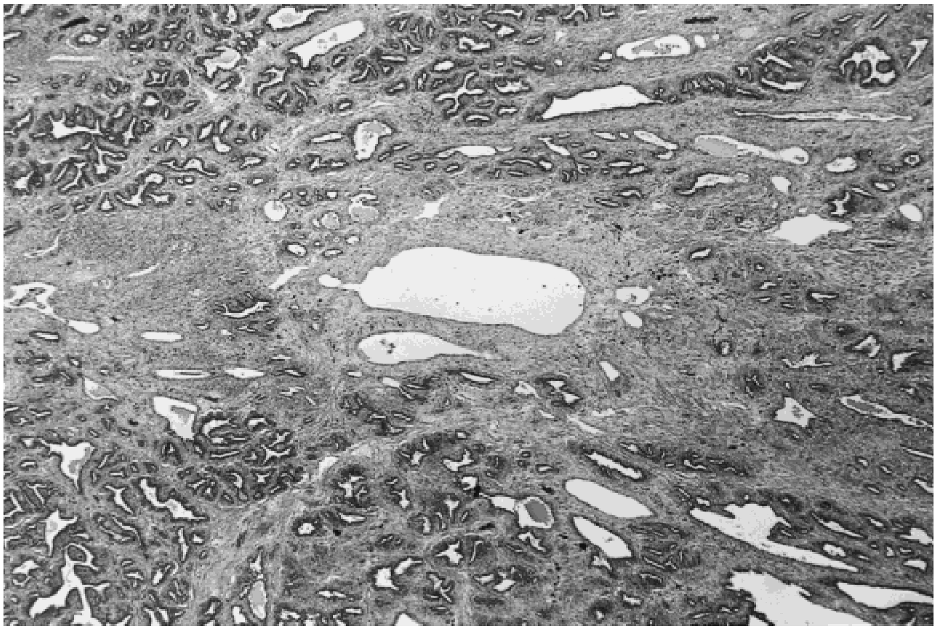

Fig. 8. Photomicrograph of the right prostatic lobe in the same dog at four weeks after TUBAL-ET. The necrotic tissue is almost absorbed, and only a small cavity remains. Hematoxylin and eosin staining, ×35.

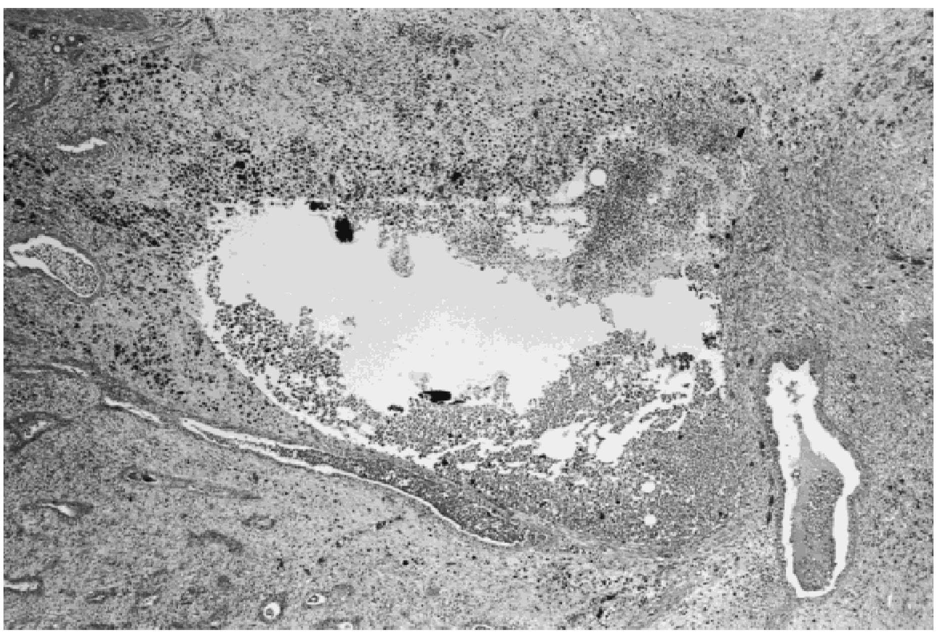

Fig. 9. Photomicrograph of the right prostatic lobe in another dog at four weeks after TUBAL-ET. The small cavity contains necrotic tissue, and histiocytes that have partly phagocytized carbon particles have invaded the area around the cavity. Hematoxylin and eosin staining, ×35.

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